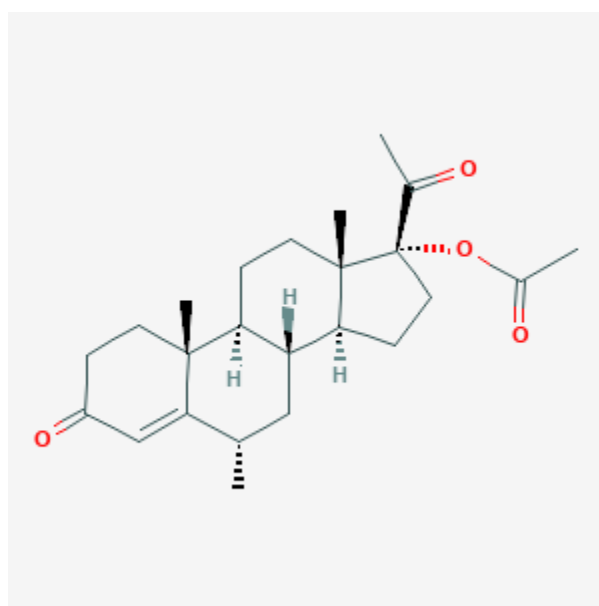




Medroxyprogesterone Acetate

Revised: October 31, 2018.

CASRN: 71-58-9



Drug Levels and Effects

Summary of Use during Lactation

Although nonhormonal methods are preferred during breastfeeding, progestin-only contraceptives such as depot medroxyprogesterone acetate (DMPA) are considered the hormonal contraceptives of choice during all stages of lactation. Fair quality evidence indicates that DMPA does not adversely affect the composition of milk, the growth and development of the infant, or the milk supply.[1][2][3][4] Some evidence indicates that progestin-only contraceptives may offer protection against bone mineral density loss during lactation, or at least do not exacerbate it.[5][6][7]

The timing of initiation of DMPA is controversial.[8] The product labeling states that it should be started no sooner than 6 weeks postpartum, based on data submitted for product approval. Studies of fair quality seem to indicate that concerns about immediate adverse effects on the infants is unfounded; however, starting too soon theoretically could affect the newborn infant adversely because of slower metabolism of the drug than older

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infants. Of concern is that no data exist on the effects of progesterone on brain and liver development at this age. Administration sooner than 6 weeks postpartum could interfere with the exclusivity or duration of lactation. A systematic review of studies using early postpartum initiation of DMPA concluded that all of the studies were of low quality and inadequate to disprove the concern about DMPA's effects on milk production if given sooner than 6 weeks after delivery.[9] A subsequent study raised the possibility of a slight reduction in breastfeeding duration in women given DMPA before hospital discharge,[10] and another study found that breastfeeding was less like to be initiated if mothers received immediate postpartum DMPA.[11]

Expert opinion in the United States holds that the risks of progestin-only contraceptive products usually are acceptable for nursing mothers at any time postpartum.[12]The World Health Organization recommends that injectable depot medroxyprogesterone acetate should not used before 6 weeks postpartum.[13]

Drug Levels

Maternal Levels. Seven women were given a single intramuscular dose of depot medroxyprogesterone acetate 150 mg 1 week after delivery. Peak milk levels occurred at varying times between days 8 to 28 after the injection, with most between 1 and 2 weeks. Peak levels ranged from 1.3 to 2.3 mcg/L. In 3 women, levels were measured 50 to 87 days after the dose and were still detectable in milk in the range of 0.54 to 0.98 mcg/L.[14]

Ten women received a single dose of depot medroxyprogesterone acetate 150 mg at 6 to 7 weeks postpartum. Breastmilk levels were measured weekly for 12 weeks. Average milk levels were highest at 1 week after injection at about 7.5 mcg/L and gradually fell to about 0.5 mcg/L at 12 weeks after the injection. The authors estimated that a breastfed infant would receive 1 to 13 mcg/day at 1 week after injection, 0.2 to 1.5 mcg/day 8 weeks after injection and up to 1 mcg/day at 12 weeks after injection.[15]

Infant Levels. Thirteen male infants whose mothers received 150 mg of medroxyprogesterone acetate intramuscularly at weeks 6 and 18 postpartum were breastfed. Complete 4-hour urine specimens were collected on 20 occasions during maternal treatment, including on the days after the injection known to have high maternal serum levels. No medroxyprogesterone or metabolites were detected by GC-MS assay (lower limit not specified) in the urine of the infants.[16]

Effects in Breastfed Infants

In a nonrandomized study, 228 women chose depot medroxyprogesterone acetate injection every 3 months as a postpartum contraceptive starting in months 2 to 4 postpartum. Eighty-eight percent of the women breastfed their infants for at least 6 months. Infants were examined during the study and again at age 4.5 years. No adverse effects on infant growth and development were noted in the exposed infants.[17]

One follow-up study of 1215 children whose mothers received depot medroxyprogesterone during nursing reported a delayed appearance of pubic hair (reported by mothers) in pubescent girls, but not boys. No other effects on growth were observed after correction for socioeconomic status.[18]

A multicenter, nonrandomized study followed 541 infants whose mothers received depot medroxyprogesterone acetate injection 150 mg every 3 months for contraception during breastfeeding. No adverse effects on infant growth through the first year were found in comparison to standard measurements.[19][20]

Thirteen male breastfed infants whose mothers received 150 mg of medroxyprogesterone acetate intramuscularly at weeks 6 and 18 postpartum were studied. No differences were found in serum levels of luteinizing hormone, follicle-stimulating hormone, unconjugated testosterone, or cortisol compared to those of a group of 9 control infants.[16]

In a nonrandomized study comparing 190 infants of women using depot medroxyprogesterone to those using a nonhormonal contraceptive or no contraception starting at about day 57 postpartum, no difference in infant

growth rates were seen from birth to 6 months of age, regardless of whether the infant was fully or partially breastfed.[21]

In a retrospective cohort study of 270 infants whose mothers were given DMPA postpartum, no effect of DMPA on weight when adjusted for cofounders and no differences between groups in psychomotor development, milestones, health problems, infant height or physical examinations.[22]

A non-blinded, randomized study of exclusively breastfeeding women compared those who received an etonogestrel implant 24-48 hours after delivery (n = 20) to those who received a 150 mg depot medroxyprogesterone acetate injection at 6 weeks postpartum (n = 20). No difference in infant weight gain was noted between the two groups.[23]

One-hundred-fifty mothers were given 150 mg of depot medroxyprogesterone acetate intramuscularly after breastfeeding was established postpartum, but before discharge at 2 to 10 days; a second dose was given at 3 months postpartum. The growth (height and weight) and illnesses of their infants was compared to those of a control group in a case-control study. No difference between the groups was seen at 1.5, 3 and 6 months postpartum. The day postpartum when the injection was given had no effect on the outcome.[24]

Effects on Lactation and Breastmilk

Galactorrhea has been reported in nonpregnant, nonlactating women using depot medroxyprogesterone acetate (DMPA). In one case series, 3.6% of 360 adolescents who used depot medroxyprogesterone acetate as a contraceptive for at least 6 months developed galactorrhea with normal prolactin levels.[25]

Numerous studies found that the use of intramuscular depot medroxyprogesterone acetate as a contraceptive beginning at 7 days postpartum or later either has no negative effect or causes increases in the milk supply, duration of lactation or quality of breastmilk.[17][19][21][22][26][27][28][29][30][31][32] However, most of these were so seriously flawed that no valid conclusion can be drawn on the effect of early initiation on breastfeeding duration.[9]

Twenty-five women who were 6 weeks postpartum were given a single injection of 150 mg of depot medroxyprogesterone acetate. Serum prolactin levels were compared to those of 25 women who used an IUD. All women breastfed their infants to about the same extent. Basal serum prolactin levels were similar between the groups at the beginning of the study. These levels slowly decreased in the IUD group, but increased in the medroxyprogesterone group. The differences were statistically significant at 6 weeks after the start of the study. Basal prolactin increases in the medroxyprogesterone were 14% over baseline and 59% over the IUD group at 6 weeks.[33]

Women (n = 80) were assigned randomly to receive intramuscular depot medroxyprogesterone acetate (DMPA) 250 mg 1 to 2 days postpartum. Other women in the study (n = 616) were started on DMPA at 30 days postpartum. The median duration of lactation in both groups was longer in these women than the lactation duration following previous births.[34]

A nonrandomized, nonblinded study compared women who received either nonhormonal contraception (n = 56) or depot medroxyprogesterone acetate (n = 47) 150 mg intramuscularly upon discharge from the hospital. No statistical differences were found in the breastfeeding rates or percentage of women exclusively breastfeeding between the 2 groups of women at 1, 4, 8, 12 or 16 weeks postpartum.[35]

In a nonrandomized, nonblinded study comparing women who were breastfeeding at discharge, 102 postpartum women received depot medroxyprogesterone acetate (dosage not stated) in the early postpartum period (average 51.9 hours postpartum; range 6.25 to 132 hours), 181 received another progestin-only contraceptive and 138 used nonhormonal contraception. No differences in breastfeeding rates were seen at 2 and 6 weeks, but women receiving any hormonal contraceptive were breastfeeding at a lower rate (72.1% vs 77.6%) at 4 weeks

postpartum. The authors concluded that progestin-only contraception initiated in the early postpartum period had no adverse effects on breastfeeding rates.[36]

A survey of 183 women who delivered in one hospital compared those who received DMPA after delivery and prior to discharge (n = 68) to those who did not receive the treatment (n = 115). There was a slight, but not statistically significant reduction in the duration of lactation among the mothers who received the early DMPA. [10]

One-hundred-fifty mothers were given 150 mg of depot medroxyprogesterone acetate intramuscularly after breastfeeding was established postpartum, but before discharge at 2 to 10 days; a second dose was given at 3 months postpartum. In a case-control study these mothers were compared to a control group of women receiving no postpartum contraception. No difference was found between the groups in the number of nursings per day over the 6-month follow-up period, nor was there a difference in patient satisfaction in multiparous mothers compared to previous breastfeeding experience(s).[24]

Women who delivered at two teaching hospitals in South Africa were randomized to receive either DMPA or an IUD within 48 hours of childbirth. There were no differences in exclusive or partial breastfeeding rates between the DMPA and IUD users at baseline or at 1 and 3 months postpartum.[37]

Alternate Drugs to Consider

Etonogestrel, Intrauterine Copper Contraceptive, Intrauterine Levonorgestrel, Levonorgestrel Implant, Oral Levonorgestrel, Progesterone

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Substance Identification

Substance Name

Medroxyprogesterone Acetate

CAS Registry Number

71-58-9

Drug Class

Breast Feeding

Lactation

Contraceptive Agents, Female

Contraceptives, Oral, Synthetic

Hormones

Progesterone Congeners